

REMARKS

Claims 1 to 7, 9 to 15, 19 and 22-27 are pending in this re-issue application. None have been allowed.

Applicants gratefully acknowledge that their previous amendments and arguments filed on January 2005 were deemed to be persuasive to overcome the rejections previously applied. However, while those rejections were withdrawn, new rejections have been made.

At the bottom of page 2 of the Action, the Examiner objects to the claims as filed, on the basis that they do not comply with 37 CFR 173(b). The Examiner directs Applicants attention to the following portions:

(2) **Claims.** An amendment paper must include the entire text of each claim being changed by such amendment paper and of each claim being added by such amendment paper. For any claim changed by the amendment paper, a parenthetical expression “amended,” “twice amended,” etc., should follow the claim number. Each changed patent claim and each added claim must include markings pursuant to paragraph (d) of this section, except that a patent claim or added claim should be canceled by a statement canceling the claim without presentation of the text of the claim.

(c) **Status of claims and support for claim changes.** Whenever there is an amendment to the claims pursuant to paragraph (b) of this section, there must also be supplied, on pages separate from the pages containing the changes, the status (i.e., pending or canceled), as of the date of the amendment, of all patent claims and of all added claims, and an explanation of the support in the disclosure of the patent for the changes made to the claims.

(d) **Changes shown by markings.** Any changes relative to the Patent being reissued which are made to the specification, including the claims, upon filing, or by an amendment paper In the reissue application, must include the following markings:

- (1) The matter omitted by re-issue must be enclosed in brackets; and
- (2) The matter to be added by reissue must be underlined, except for amendments submitted on compact discs (§§and 1.821(c))...

The Examiner specifically states that “The Amendment does not comply because applicants have filed a “claim listing” and a “marked up copy” which is no longer required.

Applicants need to submit a single listing which shows all of the changes made according to 1.173(b).” Applicants respectfully submit the present amendment fully addresses this concern. Applicants point out, however, that instead of “Once amended” or “twice amended” for example, applicants have used terminology such as “currently amended” or “previously amended” and “previously presented”, which applicants respectfully submit is more informative.

At the middle of page 4 of the Action, the Examiner states that the reissue oath is defective on the basis that applicants failed to provide the residence address/ mailing address of each and every inventor. In response, applicants hereby submit a new reissue Declaration in which the address of each of the inventors is included.

At the bottom of page 5 of the Action, The Examiner rejects claims 1-3, 6-7, 11 14, and claims 4-5, 12-13 and 15 as indefinite. The Examiner states:

Claims 1-3, 6,-7, 11 and 14 are drawn to an assay for determining the COX-2 activity “of a sample” comprising the steps of adding a cell preparation (which is actually the source of the COX enzyme), a sample comprising COX-2 inhibitor and arachidonic acid followed by measuring the amount of PGE produced. The step (a) is highly confusing to the Examiner because it is not clear whether the “sample” in the preamble of the claims and the “sample” in step (2) of (a) are one and the same. If they are one and the same, then it is not clear to the Examiner as to how one of ordinary skill in the art can expect to test the activity of the sample having an inhibitor of the enzyme. It is not clear whether applicants meant to claim an assay to determine the “COX-2 *inhibitory* activity of a sample”, wherein the said sample comprises a putative COX-2 inhibitor. On the other hand if applicant did not mean the above, Examiner requests clarification.

The Examiner continues:

While that may all be so, will the way applicant has written the claim leads to the confusion with respect to the source of the enzyme for the assay. As is, the claims suggests that the source of the enzyme is the sample and one is measuring the COX-2 activity in same sample. However, upon closer examination of

the assay, it becomes clear that the “sample” is not the source of the enzyme and that it is the osteosarcoma cell preparation that is the source of the enzyme and said “sample” indeed is the source for the inhibitor. Therefore, as suggested by the Examiner in the previous office action and in the instant Office action, applicant is urged to review the claim language. Perhaps, applicant meant to recite “An assay for determining the COX-2 inhibitory activity of sample”. The “sample” is the one comprising the putative COX-2 inhibitor and it is that inhibitor that is being assayed for its potential to inhibit COX-2. Either way, Examiner urges applicant to clarify the issue of COX-2 enzyme source for the assay, as to whether the enzyme comes from the “sample” or from the osteosarcoma cell preparation.

It is Applicants understanding that source of the issue being raised by the Examiner is that the preamble of the claims at issue describe the invention as “An assay for determining the cyclooxygenase-2 activity of a **sample...**” (Emphasis added.) However, in step (a)2, the term “sample” is used in a different way. As shown in the Examples, a human osteosarcoma cell preparation, a sample comprising a putative cyclooxygenase-2 inhibitor, and arachidonic acid are combined into a composition and the amount of prostaglandin E₂ produced in the resulting composition is determined. Applicants have amended the claims to more clearly point this out.

At the bottom of page 7 of the Action, the Examiner rejects claims 19, 26 and 27 as indefinite. The Examiner states:

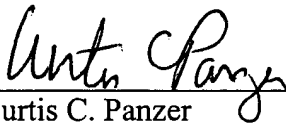
Claim 19(b) refers to sequences in figures and recites specific SEQ ID NO in parentheses. Such a depiction is confusing and unclear to the Examiner. This is because applicants do not provide a SEQ ID for the sequences depicted in the figure and therefore it cannot be taken for granted that the sequences in the figures and those listed in the sequence listing with appropriate SEQ ID NO are one and the same. Examiner urges applicants to refrain from referring sequences to the figure and provide only SEQ ID NO. Correction is required.

In response applicants have amended claim 19 as requested. For completeness, applicants point out that claims 26 and 27 appear to be rejected on the basis that they depend from claim 19. Applicants respectfully submit that the amendment to claim 19 fully addresses this concern.

At the bottom of page 8, the Examiner rejects claims 9-10 as obvious over Rodan, et. al (1986). Applicants respectfully traverse. Let us assume, arguendo, that Rodino teaches the use of osteosacroma cell line for use in an assay for measuring cyclooxygenase activity. Even if so, the subject matter of claim 9 and 10 is unobvious. The Rodino protocol as characterized by the Examiner, would result in the expression and measurement of the activity which is the sum of the COX-1 related activity and the COX-2 related activity. Thus, depending on the specifics of the assay, a compound that inhibits substantial amounts of both COX-1 and COX-2, would inhibit much more cyclooxygenase in the Rodino assay, than a COX-2 selective compound. Results of that sort would not be helpful where one is trying to find discover compounds that are selective inhibitors of COX-2. In contrast claims 9 and 10, are specifically directed to osteosacroma cells which express selectively COX-2. Applicants direct the Examiner's attention to the enclosed reference by E. Wong, et. al., (1997). See, for example, the results beginning at page 53.

Having addressed all of the outstanding objections and rejections, applicants respectfully submit that the application is now in condition for allowance and passage thereto is earnestly requested. The Examiner is invited to contact the attorney at the telephone number provided below, if such would advance the prosecution of this case.

Respectfully submitted,

By 
Curtis C. Panzer
Reg. No. 33,752
Attorney for Applicants

Date: June ³/₂, 2005

MERCK & CO., Inc.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(732) 594-3199